








# Transarterial Embolization for Sporadic Renal Angiomyolipoma: Patient Selection and Technical Considerations for Optimal Therapeutic Outcomes

산발성 신장 혈관근지방종에 대한 경동맥 색전술: 최적의 치료 결과를 위한 환자 선택 및 기술적 고려 사항

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Although renal angiomyolipoma (AML) is a benign tumor, treatment may be necessary occasionally because it can cause potentially life-threatening retroperitoneal hemorrhage. Transarterial embolization (TAE) is a safe and effective treatment option to prevent the hemorrhagic rupture of AMLs and relieve the symptoms caused by enlarged lesions or active bleeding. However, there is no clear consensus regarding the indications for prophylactic TAE in patients with sporadic renal AMLs. In urgent TAE for bleeding AMLs, there is a likelihood of incomplete embolization when the focus is on stabilizing the clinical symptoms. This pictorial essay discusses the patient selection and technical considerations to achieve optimal therapeutic effects as well as the follow-up findings after TAE.

**Index terms** Angiomyolipoma; Kidney; Embolization, Therapeutic

## INTRODUCTION

Determining the timing and method of treatment for renal angiomyolipomas (AMLs)

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is a frequently encountered problem in the clinical practice as they have a gradual tendency to grow and rupture (1, 2).

AML is the most common benign mesenchymal tumor in the kidney that belongs to the family of perivascular epithelioid cell tumors (1, 3, 4). AML is histologically composed of varying proportions of dysmorphic elastin-poor vessels (angio), smooth muscle-like cells (myo), and mature adipose tissue (lipo) (1-3, 5).

These various kinds of different pathologic features between the lesions eventually affect the heterogenous radiologic appearances that lead to a wide spectrum of clinical behaviors: from an asymptomatic AML with negligible growth rates to an AML with a life-threatening retroperitoneal hemorrhage (1, 3, 5).

Sporadic AML accounts for 80% of renal AMLs, which occurs in 0.2%–0.4% of the general population (1, 3, 4). The remaining approximately 20% are associated with tuberous sclerosis complex (TSC), and AMLs are observed in 55%–90% of patients with TSC (1-3). In sporadic cases, AMLs are usually solitary, and exhibits a female predominance (1).

The main clinical concern over sporadic AMLs is the bleeding risk of the lesion and being the target of the management strategy (4). Given the benign nature of AMLs excluding the potentially malignant epithelioid AMLs, nephron-sparing approach is the cardinal principle including: active surveillance, transarterial embolization (TAE), ablation and nephron-sparing surgery (1, 3, 4, 6).

Surgery nowadays tends to be reserved and proceeds in case of a diagnostic uncertainty (5, 6). TAE is widely and increasingly used as a primary treatment for AMLs, because the procedure is minimally invasive and preserves renal function with a high success rate (6). But, some researchers have questioned about how the TAE outcome will have an effect in the long-term for AMLs (1, 7). In addition, general indications of prophylactic TAE for sporadic AMLs have not been clearly established and there is no standard protocol for the procedure (2, 5).

In this article, the indications and patient selection of TAE for sporadic renal AMLs are presented based on the authors' experience of the procedure and literature review. Authors also described the technical tips of TAE for achieving better clinical outcomes, the strategies for avoiding procedure-related complications and the patient's post-embolization follow-up.

## DIAGNOSIS

The majority of renal AMLs are now incidentally detected on imaging studies underwent for other reasons (5). When a solid renal tumor encountered in an adult, the identification of fat using CT or MRI enables a confident diagnosis of a classic AML (3, 4). Fat poor AMLs can represent a diagnostic challenge, which often require the differentiation from renal cell carcinomas (RCC) (3, 4).

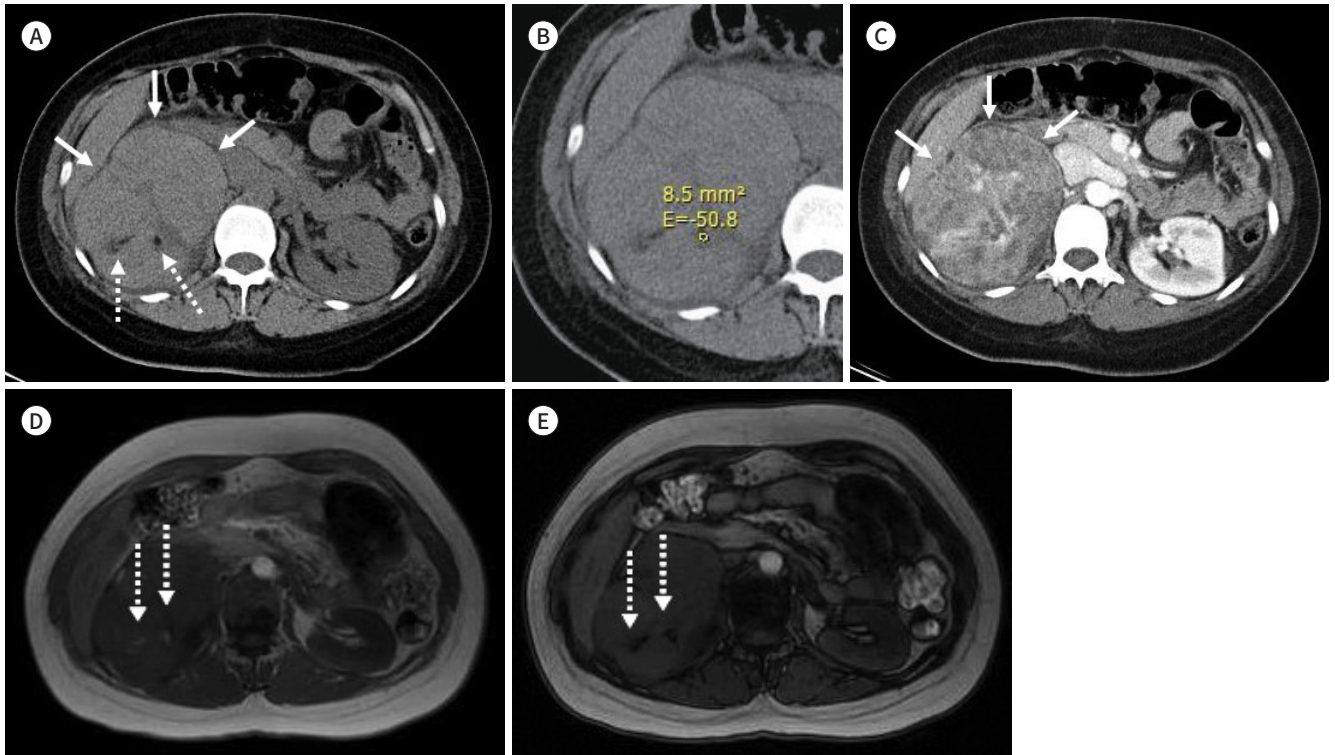
On an unenhanced CT, a hypodense area containing attenuations less than -10 Hounsfield unit is considered diagnostic of macroscopic fat (3, 4). An acquisition of a thin (less than 3 mm) slice thickness and obtaining attenuation measurements using small regions of interest (ROI) or even pixel values allow to detect a small amount of fat within AMLs (Fig. 1) (3). The high attenuation blood by intralesional hemorrhage may mask the characteristic of a fat

**Fig. 1.** A 27-year-old female with an incidentally discovered angiomyolipoma.

**A-C.** CT shows an exophytic mass (arrows) with heterogeneous enhancement (**C**) in the upper polar area of the right kidney, and small regions of interest containing fat attenuation (dashed arrows) in the unenhanced scan (**A**) and its magnified image (**B**).

**D, E.** T1-weighted in-phase (**D**, TR: 3.47, TE: 2.303) and opposed-phase (**E**, TR: 3.47, TE: 1.151) MRI show a decrease in the signal intensity (dashed arrows) within the tumor.

TE = echo time, TR = repetition time



component (3).

MRI is also used for detecting a fat area by using a T1-weighted imaging with a frequency selective fat suppression. A frequency selective fat suppression generally indicates the presence of fat cells in the lesion (3, 4). Chemical shift fat suppression is more helpful for detecting a small amount of fat (Fig. 1). However, chemical suppression of MRI cannot distinguish the fat cells in AMLs from cells containing intracytoplasmic fat in the clear cell RCC. The signal loss (a sharp black boundary; “india ink artifact”) at the border of the mass and renal parenchyma is an AML indicative (3, 4). Compared to this, the chemical shift suppression throughout the mass can be seen in both clear cell RCC and AML with small amount of fat cells dispersed throughout the mass (3). Another clue suggestive of fat poor AML over RCC is relative to T2 hypointensity of the lesion (4).

## PATIENT SELECTION FOR PROPHYLACTIC TAE

For the management of incidentally detected and asymptomatic AMLs, the issues of active surveillance versus intervention are frequently encountered in the clinical practice.

More than 90% of patients are asymptomatic at the time of diagnosis (5, 8). The majority of sporadic renal AMLs are clinically insignificant and do not require any immediate interven-

tion, because they remain asymptomatic with negligible growth rates (1, 3, 8). However, some grow continuously over the course of time and rupture, resulting in a life-threatening retroperitoneal hemorrhage (2, 3, 5).

It is known that a tumor size is one of the important factors contributing bleeding (9). Traditionally, treatment has been often recommended for renal AMLs larger than 4 cm since Oesterling et al. (10) proposed a renal AML management strategy based on tumor size and symptoms (3, 10). This size criterion is based on several retrospective studies showing that tumor size larger than 4 cm was found to have a positive correlation with the occurrence of AML rupture (4, 10).

However, in subsequent studies, some investigators have proposed to increase the size threshold (4 to 6 cm or 8 cm) (4, 5, 11). Ouzaid et al. (12) investigated retrospectively the outcomes of patients with AMLs managed by active surveillance. The authors described that among 38 patients with tumors larger than 4 cm, 66% could be maintained on surveillance, suggesting the likelihood of overtreatment occurring by the traditional size criteria.

Bhatt et al. (8) published a large series study on the natural history of renal AMLs and described that only 30% of lesion larger than 4 cm were symptomatic and they do not require an early intervention based on the size alone. Lee et al. (9) reported that the optimal size cut-off point predicting hemorrhage in sporadic AML was 7.35 cm. In their study, the bleeding rate of AML  $\geq$  4 cm and  $<$  4 cm were 23.6% and 4.8% respectively. To date, there is no clear consensus to determine the ideal patients to undergo TAE for asymptomatic renal AMLs and the existing 4 cm cut-off does not seem to accurately reflect the risk of bleeding (3, 4, 13).

The more important factor is thought to be intralesional saccular aneurysm (Fig. 2) (2, 5). A positive correlation between the size of aneurysm and hemorrhage has been observed (3, 4, 14). In the findings from a study by Yamakado et al. (14), aneurysm larger than 5 mm was found to predict spontaneous hemorrhage with a 100% sensitivity and 86% specificity, whereas a tumor size of 4 cm or larger resulted in 100% sensitivity and 38% specificity.

When deciding whether to treat with TAE or not, the composition of the AMLs should be evaluated with the imaging study. The specific target of embolization is angiomyogenic component, which is the main cause of bleeding complication (Fig. 3) (2).

The composition is closely related to the vascularity seen in angiography. In a study investigating the vascularity of renal AMLs larger than 4 cm, the group of minimal vascularity was significantly less likely to bleed, and did not require an intervention than the group of marked vascularity (15).

Even if the tumor is rather large, TAE is not the optimal treatment for nearly pure fatty AMLs without both angiomyogenic component and aneurysmal dilatation of the feeding vessels. Tumor volume reduction through TAE cannot be expected, because fat component is resistant to embolization (Fig. 4) (2, 5, 16).

The above-mentioned radiologic factors predictive of the spontaneous bleeding in renal AMLs need to be addressed at preprocedural imaging studies during active surveillance (Table 1).

In addition to these radiologic parameters, clinical factors should be considered as well (Table 1). Pregnancy is a clinical risk factor causing predictive bleeding in renal AMLs. Overexpression of estrogen, progesterone, and androgen receptors has been found in AMLs, sug-

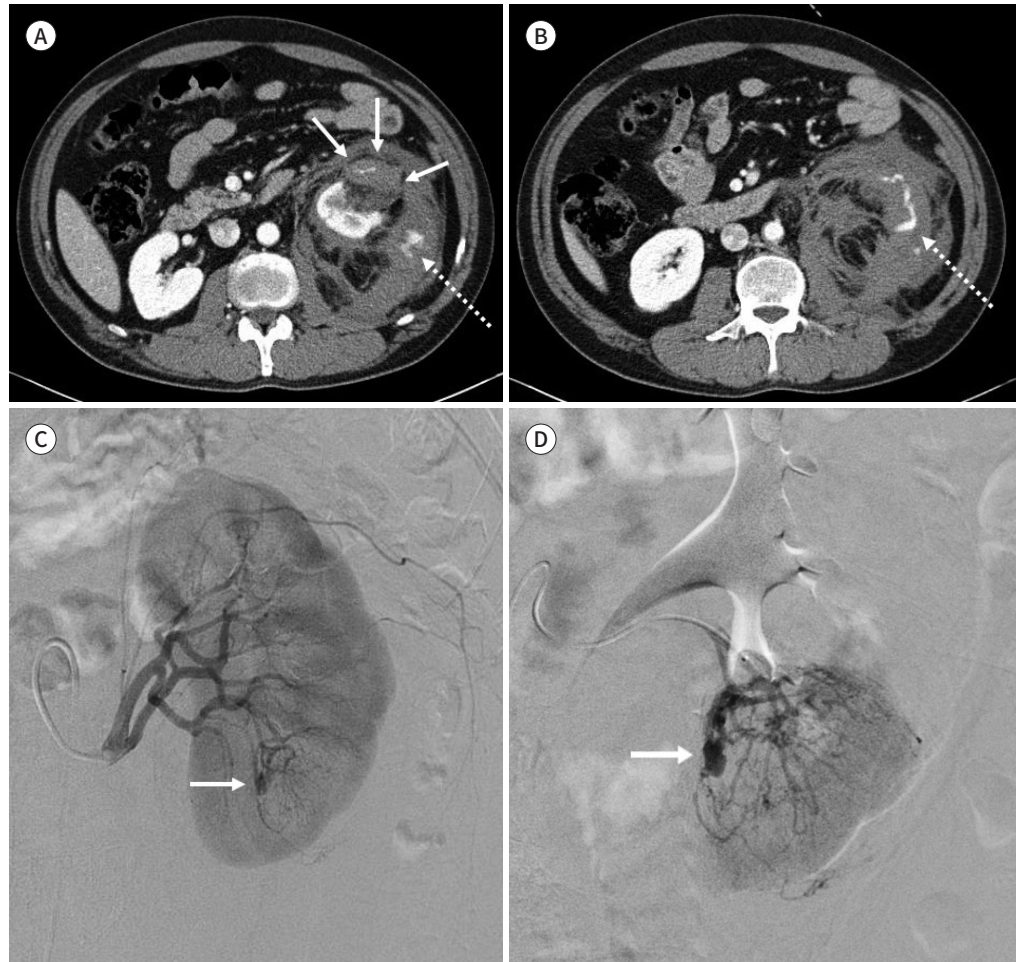


**Fig. 2.** A 50-year-old male with bleeding angiomyolipoma.

**A, B.** Enhanced CT shows an exophytic, fat-containing renal mass (arrows) with intralesional and perirenal hematomas and contrast extravasations (dashed arrows), and the maximum diameter of the tumor barely exceeds 4 cm; however, intralesional hyperdense blood limits the assessment of the presence of aneurysms and tumor composition.

**C.** Angiogram of the left renal artery trunk after one day reveals tumor staining with abnormal vasculature (arrow).

**D.** Selective angiogram of the tumor-feeding vessel using a microcatheter shows a better view of the pseudoaneurysm (arrow), and unlike the CT images, the angiogram does not show contrast extravasation. Selective transarterial embolization was performed using polyvinyl alcohol (150–250  $\mu$ m) and microcoils (not shown).



gesting that they are sensitive to hormones (4, 5, 17). Besides, both circulating blood volume and renal flow increases during the pregnancy (5, 17). Therefore, the tumor may present an increase in growth rate and the possibility of hemorrhagic rupture during pregnancy. More aggressive prophylactic treatment of AMLs may be justified in women of childbearing age, in order to prevent maternal and fetal morbidity in future pregnancy (4, 5, 17, 18), and considering for prolonged exposure to hormones for the rest of their life.

Furthermore, it is likely that determining TAE should be based on the personalized treatment recommendations considering patient-specific factors (Table 1). Prophylactic TAE could be more beneficial for older patients and those with poor renal or physiologic reserves

Table 1. Considerations prior to Performing TAE for Renal AMLs

Radiologic risk factors predictive of bleeding	
Tumor size larger than 6–8 cm	The existing size criteria (4 cm) tends to be adjusted upwards Aside from overall tumor size, other factors should be assessed together
Intralesional saccular aneurysm	Aneurysm larger than 5 mm is a more specific predictor of bleeding than overall tumor size
Enhancing areas within the tumor	Enhancing portion indicates angiomyogenic component, which is the main cause of bleeding and the target of embolization
Symptomatic AMLs	
Hemorrhage	Urgent TAE should be discussed as the first-line treatment Hemorrhagic rupture with extrarenal retroperitoneal extension may lead to unstable vital sign
Pain	Pain may be caused by compressive effect by enlarging lesion itself or active bleeding
Obstructive uropathy	Massive lesion can cause blockage of urinary collecting system
Clinical settings for the patient	
Female of childbearing age	Pregnancy is the known risk factor of tumor growth and rupture Prophylactic management should be considered for prolonged exposure to hormones and the future pregnancy
Low renal reserve	Hemorrhagic rupture can cause renal insufficiency in patient with low capacity of kidney function such as solitary kidney or underlying medical renal disease
Poor physiologic reserve	Patients with a lack of physiologic reserves are not tolerated in sudden bleeding and surgical treatment
Low accessibility of emergency medical treatment	Retroperitoneal hemorrhagic rupture in AMLs can be life-threatening and requires emergent treatment

AML = angiomyolipoma, TAE = transarterial embolization

who cannot tolerate bleeding events and surgery (5, 19). Prophylactic TAE can also help patients in an isolated area and specific situations where emergency care is not accessible (5).

## SYMPTOMATIC AND BLEEDING AMLS

Symptomatic AML is the indication of intervention regardless of tumor size (Table 1). TAE is a first-line treatment in renal AMLs with active bleeding in which surgery is generally reserved (2, 4, 5).

Hemorrhage may be confined to the inside of the tumor without extrarenal extension (Fig. 3). But, intratumoral bleeding continues to increase pressure within the tumor, resulting in rupture, which may lead to hematuria or retroperitoneal hemorrhage (Fig. 2).

When the amount of bleeding loss is not large, patients often complaint of only severe flank or back pain, and the symptoms and signs of hemorrhagic shock may not be evident.

However, when the blood loss is massive due to rupture with extrarenal retroperitoneal extension of bleeding, the vital signs can become unstable. As from the previous reports, 11%-20% of ruptured AML have presented with hemodynamic instability (5).

Prompt management with TAE allows rapid stabilization of vital signs and can help to reduce the amount of blood transfusions and obviate the need for subsequent surgery (7). Even the hematoma is localized inside the tumor and accompanied by no contrast extravasation on cross-sectional imaging study, urgent TAE is necessary to arrest ongoing bleeding, interrupt retroperitoneal extension of hemorrhage and prevent rebleeding. It is also helpful for

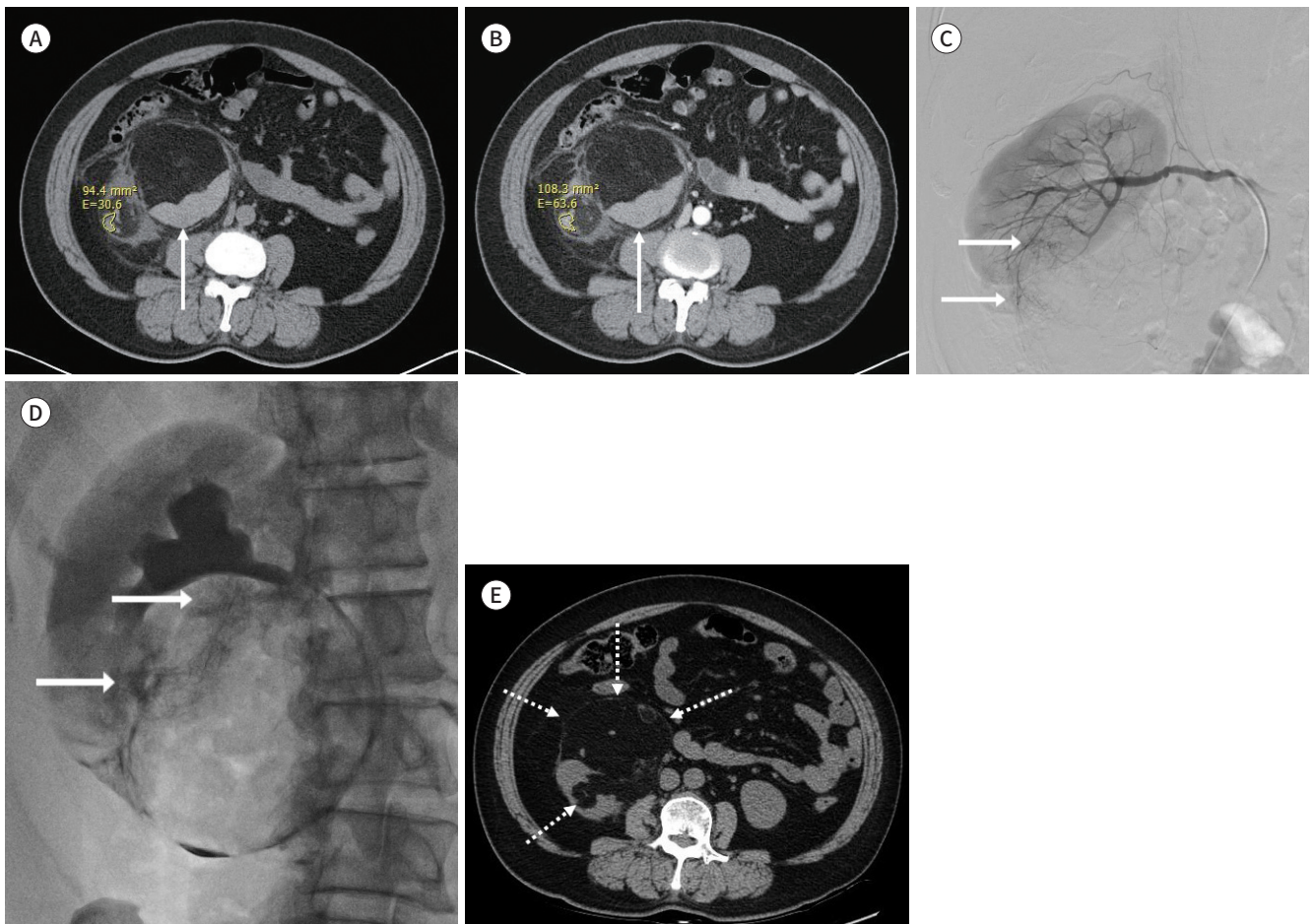
an immediate pain relief in patients with bleeding AMLs.

Very little bleeding can be subclinical or missed (5). In our experience, some patients experience previous episode of flank or back pain days to months before AML hemorrhagic rupture occurs, which is thought to be an event of the preceding intratumoral microbleeding. Persistent pain or discomfort may be related to the compressive effect of enlarging tumor itself. TAE is also considered in patients with a painful AML, regardless of the tumor size.

### FEEDING ARTERIES SUPPLYING RENAL AMLS

Renal AMLs are usually vascularized by feeding vessels derived from segmental artery of

**Fig. 3.** A 54-year-old female with angiomyolipoma bleeding caused by a small angiomyogenic component. **A, B.** Initial CT shows a renal fatty mass measuring 11 cm × 10 cm × 9 cm with an intralesional hematoma (arrows), and the unenhanced (**A**) and enhanced (**B**) axial scans show a small area of enhancement (yellow circles); however, intralesional hyperdense blood limits the evaluation of the tumor composition. **C.** Right renal artery angiogram reveals subtle tumor staining (arrows) without aneurysm or contrast extravasation. Selective embolization was performed using a mixture of ethanol and lipiodol (7:3) (not shown). **D.** Spot fluoroscopy after embolization shows partial accumulation and stasis of the contrast agent (arrows), probably indicating an angiomyogenic component. **E.** Unenhanced CT after 3 years shows a residual fatty mass without an intralesional enhancing area (dashed arrows), with a decrease in the tumor volume by 28.51%.





the renal artery that supply the renal parenchyma (Fig. 5) (7). The renal arteries are paired and arise at nearly right angles off of the both sides from abdominal aorta at the first to second lumbar vertebral body level, just below the superior mesenteric artery. There may be one or more renal arteries supplying in each kidney which are easily identified by enhanced CT scans.

Although the mechanism of the bleeding propensity is speculative, the feeding vessel walls histologically lack poor elastic layers and have disorganized adventitial cuff of smooth muscle. The vessels are eccentrically thick-walled, fragile, aneurysmal, and prone to rupture (4, 5, 7, 10).

AMLs exhibit heterogenous angiographic features according to the proportion of angiomyogenic and fat component. Nearly pure fat AMLs display small and stretched feeding vessels without evident tumor opacification (Fig. 4) (15). Angiomyogenic component shows opacification and hypervascularity with numerous coiled feeding vessels (Fig. 6) and tortu-

**Fig. 4.** A 58-year-old female with almost fat angiomyolipoma.

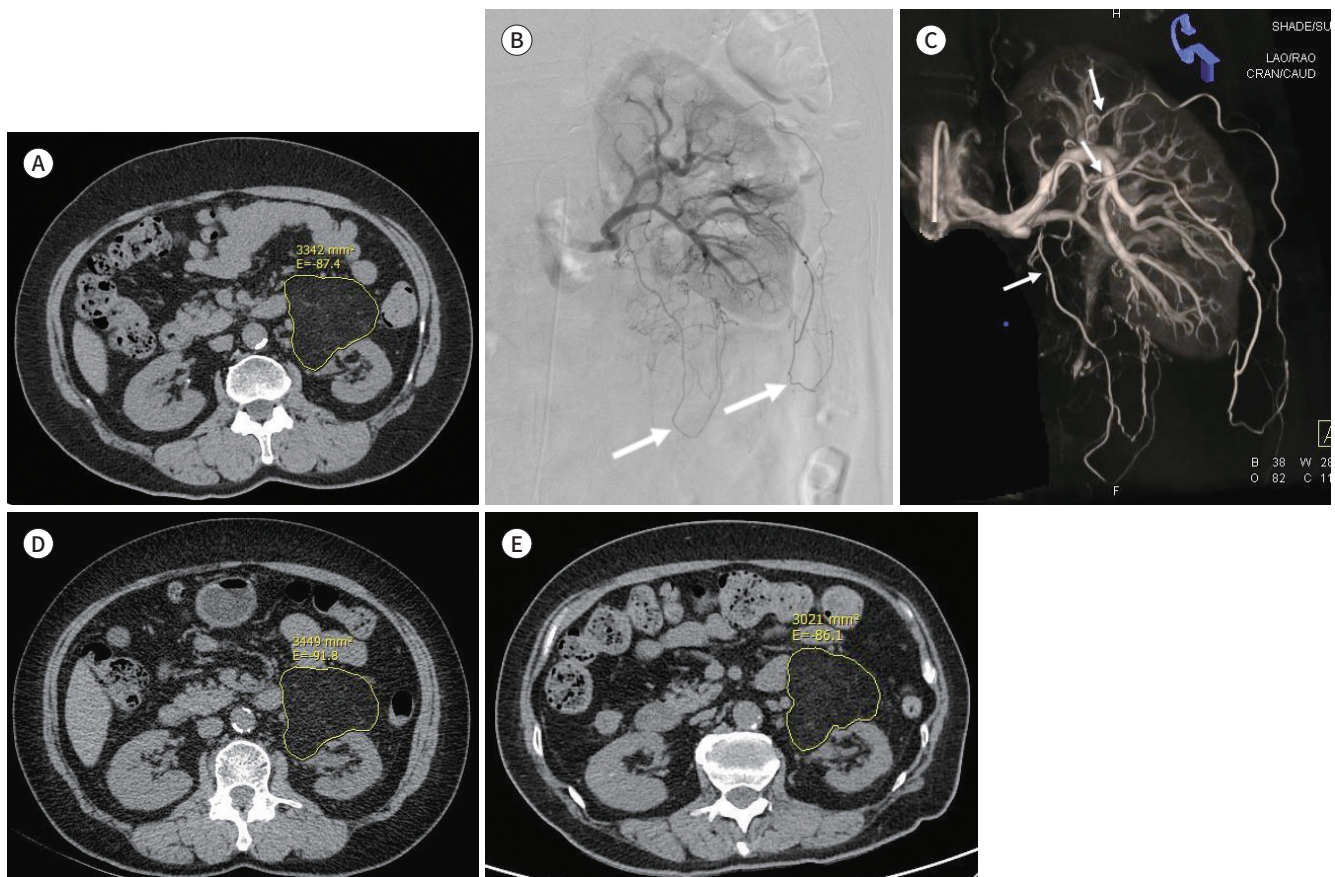
**A.** Preprocedural CT shows a fatty mass in left kidney, with a maximum diameter of 8 cm.

**B.** Left renal artery angiogram shows few small and stretched feeding vessels (arrows) supplying the angiomyolipoma without tumor opacification.

**C.** Volume-rendering image of the C-arm cone-beam CT reveals that all the feeding vessels (arrows) originate from the segmental arteries of the renal artery. Selective TAE was performed using a mixture of alcohol and lipiodol (7:3) and polyvinyl alcohol (150–250  $\mu$ m) (not shown).

**D, E.** Postprocedural unenhanced CT performed 1 year (**D**) and 5 years (**E**) after TAE show no significant change in the tumor size.

TAE = transarterial embolization





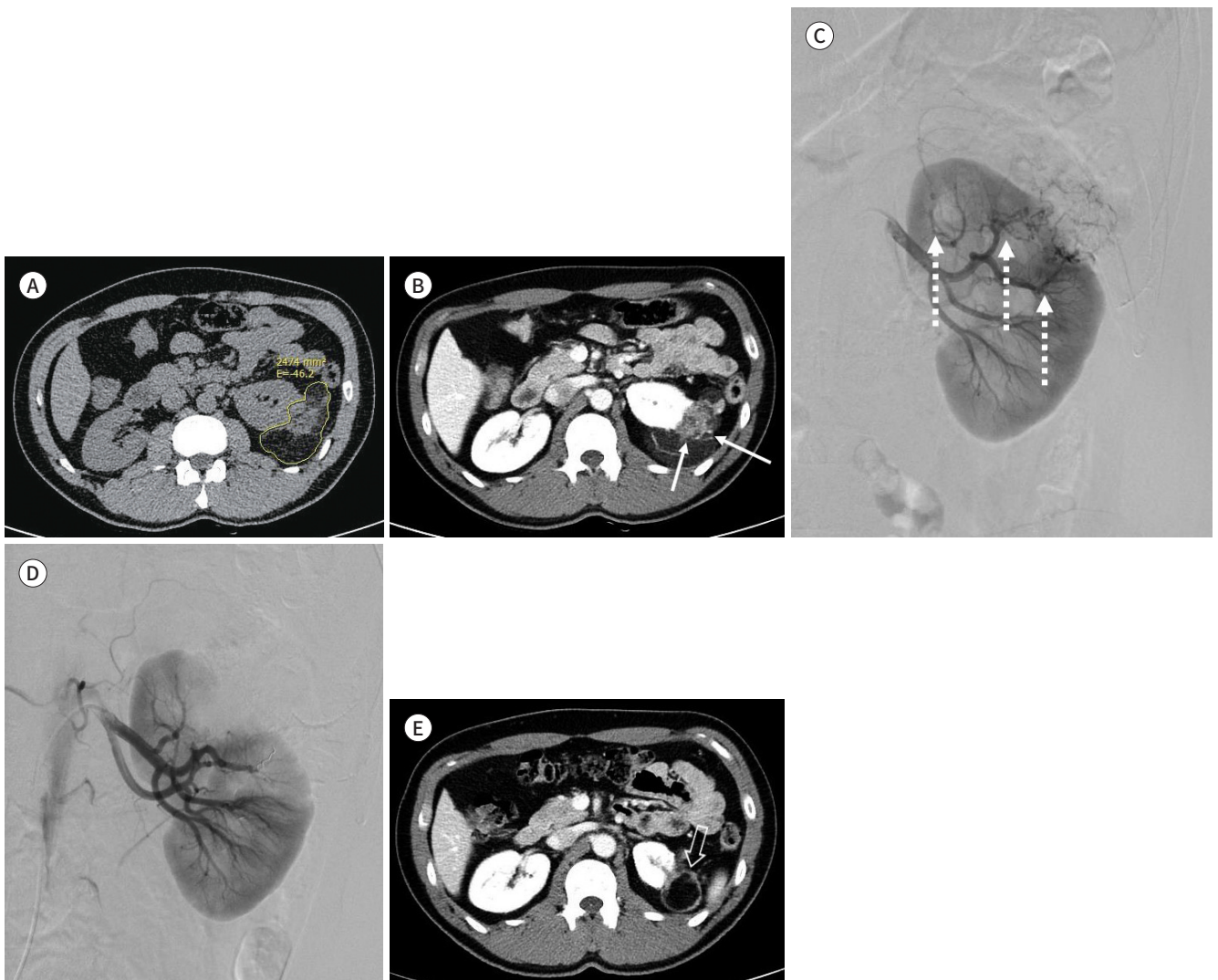
ous enlarged vessels (Fig. 7) with or without aneurysm (15).

Aside from intrarenal branches of renal arteries, AMLs can be supplied from extrarenal branches originating from the renal artery, such as the renal capsular artery, the inferior adrenal artery (Fig. 7), and the ureteral artery. In addition, the potential feeders can originate from the aortic branches, such as the middle adrenal artery, the ureteral artery, the gonadal artery, the lumbar artery, the intercostal artery, and the inferior mesenteric artery (Table 2) (20-22).

Unidentified and missed extrarenal feeders can cause incomplete devascularization, which can lead to tumor regrowth or rebleeding after TAE (21). Determining the presence of

**Fig. 5.** A 45-year-old male with asymptomatic angiomyolipoma.

- A, B.** Preprocedural CT shows an exophytic fatty mass measuring 8.5 cm × 6.0 cm × 6.0 cm, with an enhancing portion (arrows) in the left kidney.
- C.** Left renal artery angiogram shows abnormal vasculature, indicating feeding vessels arising from the segmental arteries (dashed arrows) of the renal artery. Selective embolization was performed using polyvinyl alcohol (150–250 μm) and microcoils (not shown).
- D.** Post-embolization angiogram shows complete devascularization of the tumor.
- E.** Enhanced CT after 3 years shows a marked reduction in size with the residual tumor composed of only fat (arrow), complete disappearance of the angiomyogenic component, and a decrease in the tumor volume by 71.01%.



**Fig. 6.** A 36-year-old female with a 12-year follow-up after prophylactic TAE for an asymptomatic angiomyolipoma.

**A.** Initial CT shows an exophytic heterogenous mass measuring 5.5 cm × 5.0 cm × 6.0 cm with a dense angiomyogenic component (star).

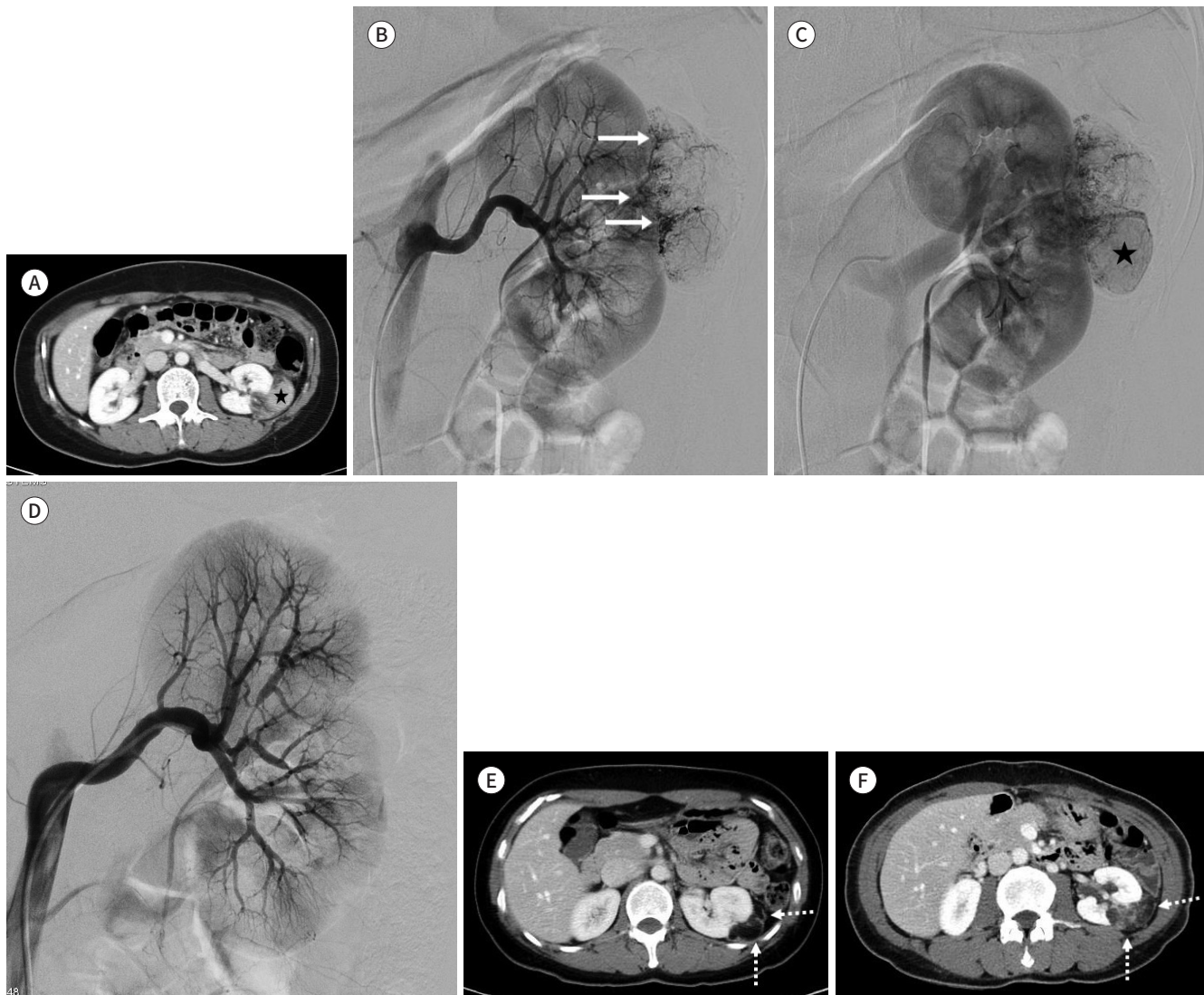
**B, C.** Left renal artery angiogram reveals numerous coiled neoplastic feeding vessels (arrows on arterial phase, **B**) and relatively denser opacification (star on venous phase, **C**), matching the CT findings.

**D.** Angiogram after selective TAE with polyvinyl alcohol (250–355 μm) shows complete devascularization of the tumor.

**E.** Enhanced CT after 4 months shows a mild reduction in size (3 cm × 2 cm × 2 cm) and a marked decrease in the attenuation of the lesion (dashed arrows).

**F.** Twelve years after TAE, the lesion shows a mild regrowth of 3.5 cm × 2.5 cm × 3.5 cm with a recurrent angiomyogenic component (dashed arrows).

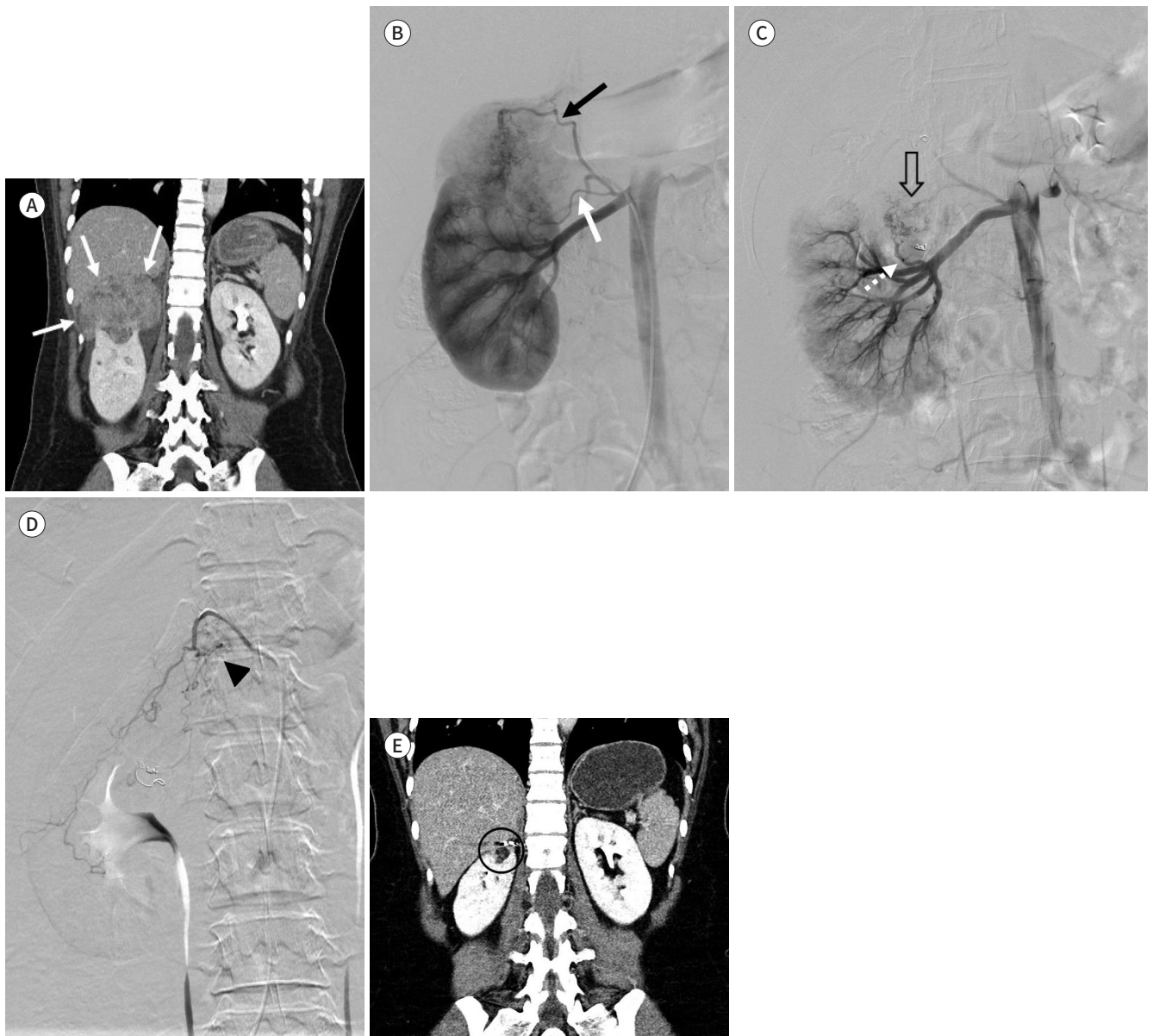
TAE = transarterial embolization



extrarenal feeding vessels is sometimes challenging. In a study to investigate factors predicting the presence of extrarenal feeders to renal AMLs, it was reported that large tumor size was a significant factor, showing that extrarenal feeders were present in 0%, 21%, and 79% of the AMLs ≤ 6.5 cm, AMLs 6.6–10.5 cm, and AMLs > 10.5 cm, respectively. Authors described that there were no significant differences between AMLs with and without extrarenal feeders in terms of patient age, tumor location, and the etiology (sporadic or TSC-related) (21).

**Fig. 7.** A 27-year-old female with a fat-poor angiomyolipoma vascularized by predominantly extrarenal feeding vessels (same case as that presented in Fig. 1).

- A.** Initial coronal CT shows an exophytic enhancing mass (arrows) measuring 10.0 cm × 9.5 cm × 8.0 cm in the upper polar area of the right kidney.
- B.** Right renal artery angiogram reveals tumor opacification supplied by the enlarged inferior adrenal artery (black arrow) and the renal capsular artery (white arrow) arising from the extrarenal portion of the right renal artery trunk. Selective transarterial embolization was performed using polyvinyl alcohol (150–250 μm) and microcoils (not shown).
- C.** Immediate follow-up angiogram shows the remaining tumor staining (arrow) supplied by the intrarenal feeders arising from the segmental artery (dashed arrow) of the renal artery.
- D.** Middle adrenal artery angiogram shows the residual tumor feeders (arrowhead).
- E.** CT after 2 years shows a small residual tumor composed mainly of fat (circle), with the tumor volume showing a marked decrease by 99.20%.



## PROCEDURE AND TECHNICAL CONSIDERATIONS

In general, TAE is performed via the common femoral artery access under local anesthesia. Prior to the procedure, CT is reviewed to determine the location and number of renal ar-



**Table 2.** Blood Vessels Supplying Renal Angiomyolipomas

Intrarenal artery; in the majority of cases
Extrarenal branches from renal artery
Renal capsular artery
Inferior adrenal artery
Ureteral artery*
Extrarenal branches from aorta
Middle adrenal artery
Ureteral artery*
Gonadal artery
Intercostal artery
Lumbar artery
Inferior mesenteric artery

\*The ureteral artery may originate from the renal artery or directly from the aorta.

teries, and identify the potential extrarenal feeding arteries (21). Abdominal aortography is not routinely performed.

The renal artery is catheterized with 4–5 Fr angiographic catheters (cobra-shaped catheter or reverse-curve catheter). The guiding sheath may be introduced into the renal artery according to the operator's preference. The catheter tip is placed in the renal artery trunk, and digital subtraction angiography is performed.

If the origin site of the feeding arteries to the AMLs is undistinguishable due to the overlapping blood vessels in the anteroposterior direction, it is helpful to obtain an additional angiography with oblique or craniocaudal angulation. Cone-beam CT may also be helpful in evaluation of feeding vessels during TAE (23).

Microcatheter with coaxial technique is used to cannulate the identified feeders selectively. Selective angiography for feeding arteries is additionally performed to evaluate the presence of contrast extravasation indicating active bleeding, and other vascular abnormalities including aneurysm and arteriovenous shunt, and collateral vasculature in more detail (Fig. 2).

After that, a microcatheter is then advanced distally to a suitable position in order to avoid reflux into a nontargeted vessel with a gentle hand-injection of contrast agents and manipulation of guide-wire under the direct fluoroscopic guidance.

Embolic materials (particle or liquid types) are administered slowly and carefully until the interruption of blood flow into a tumor with stasis of contrast agent is seen. A special care is needed to avoid a nontargeted embolization and an inappropriate early proximal occlusion. Additional coils can be applied to block continuous blood inflow into the feeding vessels.

Embolization of massive lesions larger than 10cm is a more difficult task because they are often supplied by multiple feeders, and it may be difficult to delineate between normal renal tissue and the lesion (24). Elaborate embolization through super-selection of all respective feeding arteries is recommended for the optimal therapeutic outcomes.

In an emergent situation of an acute bleeding, even if hemostasis occurs and the patient is stabilized through prompt TAE, embolization should be continued until complete devascularization is achieved.



Because contrast extravasation seen in the preprocedural CT may not be seen on angiography (Fig. 2), it may be difficult to localize the aneurysm responsible for the active bleeding (25, 26). In addition, an incomplete devascularization for the same or a different lesion can

**Fig. 8.** A 45-year-old female with sporadic multiple unilateral angiomyolipomas.

**A.** Initial CT to investigate the acute flank pain in the patient shows a fatty mass, measuring 10.0 cm × 8.5 cm × 11.0 cm, with intralesional and perilesional hematoma in the left kidney and nodular contrast pooling (arrow).

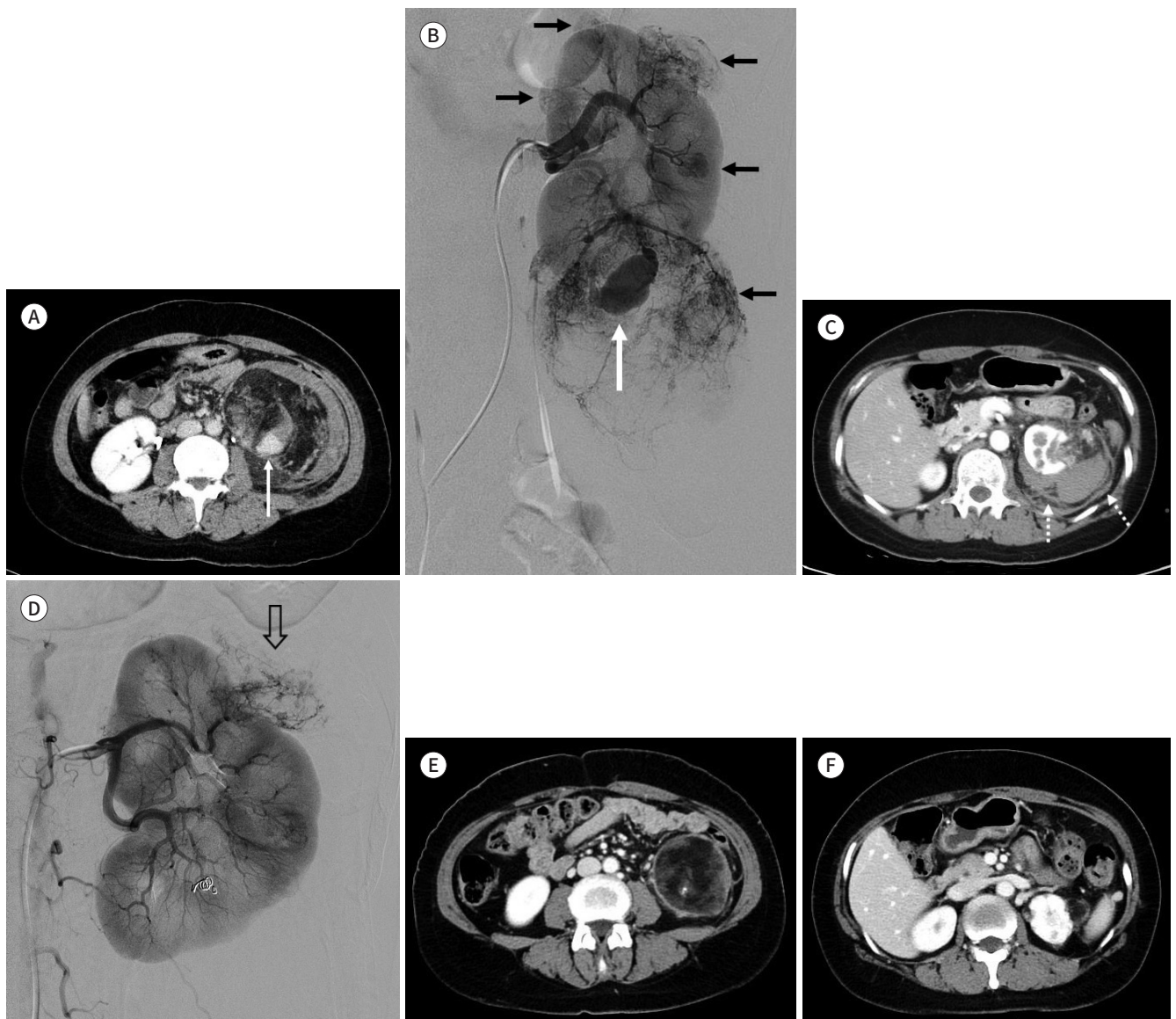
**B.** Left renal artery angiogram reveals multiple tumor opacifications (black arrows) in the left kidney, with the largest tumor of the lower pole exhibiting a large aneurysm (white arrow). Selective TAE for the largest tumor was performed using polyvinyl alcohol (355–500 μm) and microcoils (not shown).

**C.** CT after 2 years for recurring flank pain shows bleeding rupture of another angiomyolipoma (dashed arrows, measuring 4 cm × 3 cm × 2 cm) in the upper pole of the left kidney.

**D.** Left renal artery angiogram shows tumor staining in the upper pole (arrow) and complete devascularization of the previously embolized lesion in the lower pole.

**E, F.** Three years after repeat TAE, CT images show residual fatty mass without an enhancing area.

TAE = transarterial embolization



lead to a tumor regrowth and rebleeding (Fig. 8) (27).

Angiography should be obtained during and after the procedure to assess changes in tumor vascularity and the presence of arteriovenous shunts, find extrarenal feeders, and confirm devascularization of the lesion.

## EMBOLIC MATERIALS

A variety of different embolic materials have been reported for TAE of renal AMLs, with good technical and clinical success (13, 28). However, there were no randomized controlled trials to determine the ideal type of embolic materials, the adequate concentration of liquid agent, and the optimal size of particle, to our knowledge. Instead, many studies used different agents within the same case series.

Ethanol causes denaturation of endothelium and activation of the coagulation cascade, and produces permanent occlusion at the capillary and arteriolar level (25, 29). Ethanol is often used in combination with ethiodized oil (lipiodol™) because of its radiolucency, but the mixed and diluted ethanol has the disadvantage of reducing the toxic effect (2, 16, 27). Pure ethanol can be used to maximize the toxicity, but there is a risk of unaware ethanol reflux in the normal renal vessels (2).

Particulate agents act by lodging into vessels and inducing inflammatory reaction, followed by necrosis, fibrosis and occlusion in the arteriolar level (25). Polyvinyl alcohol (PVA) is a permanent embolic agent, while gelatin sponge particle is a temporary embolic agent (30). Although the ideal particle type and size is yet to be determined, the commonly used material is nonspherical PVA of 300–700  $\mu\text{m}$ . Larger particles cause proximal occlusion and induce the risk of revascularization through collateral channels. When using particulate embolic materials, a special attention is required to prevent embolic materials from plugging in the proximal portion of the feeding artery. Embolization with smaller particles may allow more distal embolization and thus more effective. However, using too small particles can lead to pulmonary complication without an effective devascularization. Villalta et al. (29) evaluated the outcomes between those who underwent TAE using agents smaller and larger than 150  $\mu\text{m}$ . Authors have demonstrated that repeated embolization of the same mass was approximately 6 times more likely to happen in those embolized with the smaller agents and 2 out of 3 patients with acute respiratory distress have also underwent embolization with the smaller agents.

Coil can optionally be used for proximal occlusion to maintain and enhance the embolic effect. Lenton et al. (26) advocated using a combination of particulate materials and coils, because the high incidence of aneurysm rupture after TAE with PVA alone was observed. But, coil should not be used alone because collateral channels feeding the tumor may be developed and the future re-access to feeding arteries will become more difficult (2, 25).

A high dilution of N-butyl cyanoacrylate in ethiodized oil can also be used. This liquid agent polymerizes and creates cast in the blood vessels. It is helpful especially in large tumors since it enables rapid distal as well as proximal occlusion (25).

Few studies recently reported that ethylene vinyl alcohol copolymer (Onyx™) came up with satisfactory results by showing no AML regrowth or rebleeding and no major complication (18, 31).

Some investigators have proposed the application of proximal balloon occlusion which was designed to prevent reflux during embolization with liquid and particles (27). But it can induce an increase in the pressure distal to the catheter tip by forceful injection of embolic materials into a closed system, resulting in aneurysm rupture (27).

Particulate and liquified materials are equally effective in achieving hemostasis for 77% to 100% of bleeding AMLs after TAE (7). There has been no proven superiority to specific embolic materials with regard to clinical results so far. Familiarity with the properties of each embolic materials will help the procedure to be safer and more effective.

## POSTPROCEDURAL ASSESSMENT

Patients are followed up at various intervals after TAE by institution. Continued active surveillance with cross-sectional imaging is necessary to assess any change in volume and composition of the tumor, and residual vascularity (5, 7). These radiological changes are the indicators of technical success for TAE.

A common index assessing the efficacy of embolization is the degree of tumor shrinkage. A meta-analysis on TAE for renal AMLs reported that the lesions were reduced in size by 30.0% (19), which may seem unsatisfactory at first glance, compared to a surgical removal.

But, the total tumor size should not be considered a risk factor for predicting bleeding after embolization, and the surgical removal of the residual tumor is not obligatory (22). The size reduction varies through TAE and correlates closely with the initial composition of triphasic component of AMLs (2, 13, 32).

Angiomyogenic components are sensitive to embolization and obliterated (Fig. 5) (22). The larger the angiomyogenic component proportion, the greater the reduction in tumor size (Fig. 7) (2, 5, 7, 32). On the other hand, fat component is usually minimally vascularized and resistant to embolization, so it is difficult to expect a reduction of tumor size in pure fatty AMLs with poor angiomyogenic component by TAE (Fig. 4) (2, 5, 16, 32).

Instead of the initial tumor composition, the initial tumor size has been suggested as a predictor for tumor shrinkage. Hongyo et al. (20) published a relatively large series including 48 prophylactic TAEs, demonstrating that tumor smaller than 7 cm was the only independent predictor of significant tumor volume reduction (50% or more) after TAE.

Tumor volume reduction gradually occurs over the course of several months and years after embolization (Fig. 9). The reduction rate begins to slow down after more than one year and appears to plateau after 3 years (2, 30, 32). Planché et al. (2) reported that the volume reduction was  $43\% \pm 32\%$  at 3 months after prophylactic TAE, with mean volume reduction rate decreasing to 5.5% per year after more than one year.

Even if the size reduction is poor, a technical success can be achieved when the vascularity and intralesional angiomyogenic component decreases clearly (Fig. 9). Re-intervention is not necessary for the residual lesion with no hypervascular enhancing portion and pseudoaneurysms. Based on our experience, the overall decrease in the attenuation of the lesion can be noted, suggesting that the angiomyogenic component dispersed throughout the tumor is responsive to TAE (Fig. 9).

Within a few days immediately after the procedure, an increase in tumor size may be ob-

**Fig. 9.** A 38-year-old female with gradual reduction in the tumor volume after transarterial embolization.

**A.** Initial CT shows a fatty mass (arrows) measuring 9 cm × 6 cm × 7 cm in the left kidney, with enhancing areas unevenly distributed within the tumor.

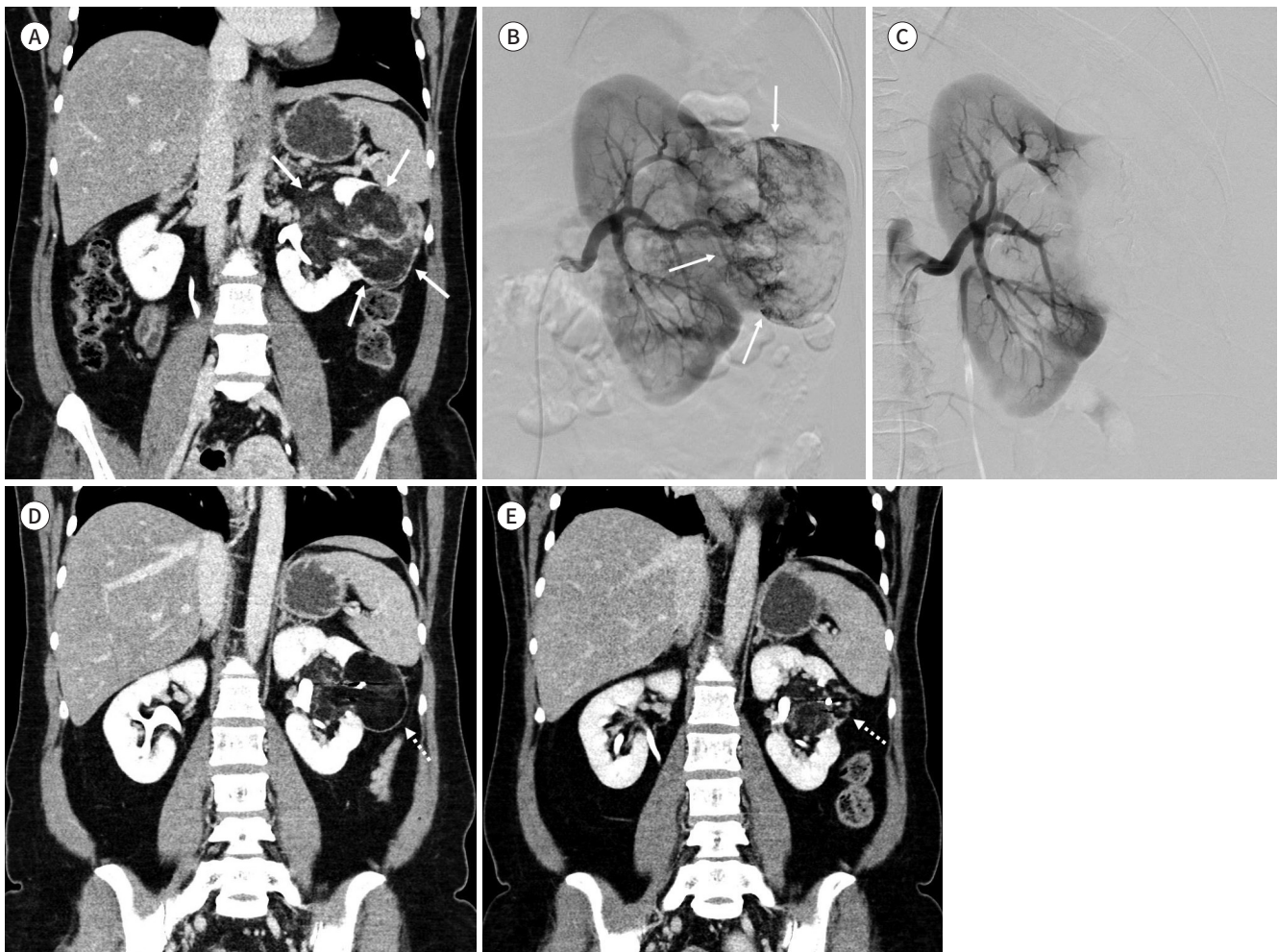
**B.** Left renal artery angiogram reveals a tumor staining with numerous coiled supplying arteries (arrows).

**C.** Angiogram after transarterial embolization with polyvinyl alcohol (150–250 μm) and microcoils shows complete devascularization of the tumor.

**D.** CT after 6 months shows mild reduction in size and a marked decrease in the overall attenuation of the lesion (dashed arrow), suggesting that embolization results in the obliteration of the dispersed angiomyogenic component.

**E.** CT after 4 years shows further reduction in the tumor size with the residual tumor mainly composed fat (dashed arrow) and a decrease in the tumor volume by 59.12%, while the average attenuation value measured on unenhanced images shows a decrease from -41.92 to -81.16 HU as compared to the preprocedural CT.

HU = Hounsfield unit



served, which is likely due to edema and inflammatory reaction (2). It is more meaningful to assess the presence and extent of the residual enhancing portion and abnormal vascularity rather than evaluating the overall tumor size during this period.

The follow-up image occasionally shows necrotic tumor with aseptic liquefaction (Figs. 10, 11), which requires differentiation from an abscess. Tumor liquefaction appears to occur primarily in large tumors with a high fat content (> 50%) (33).



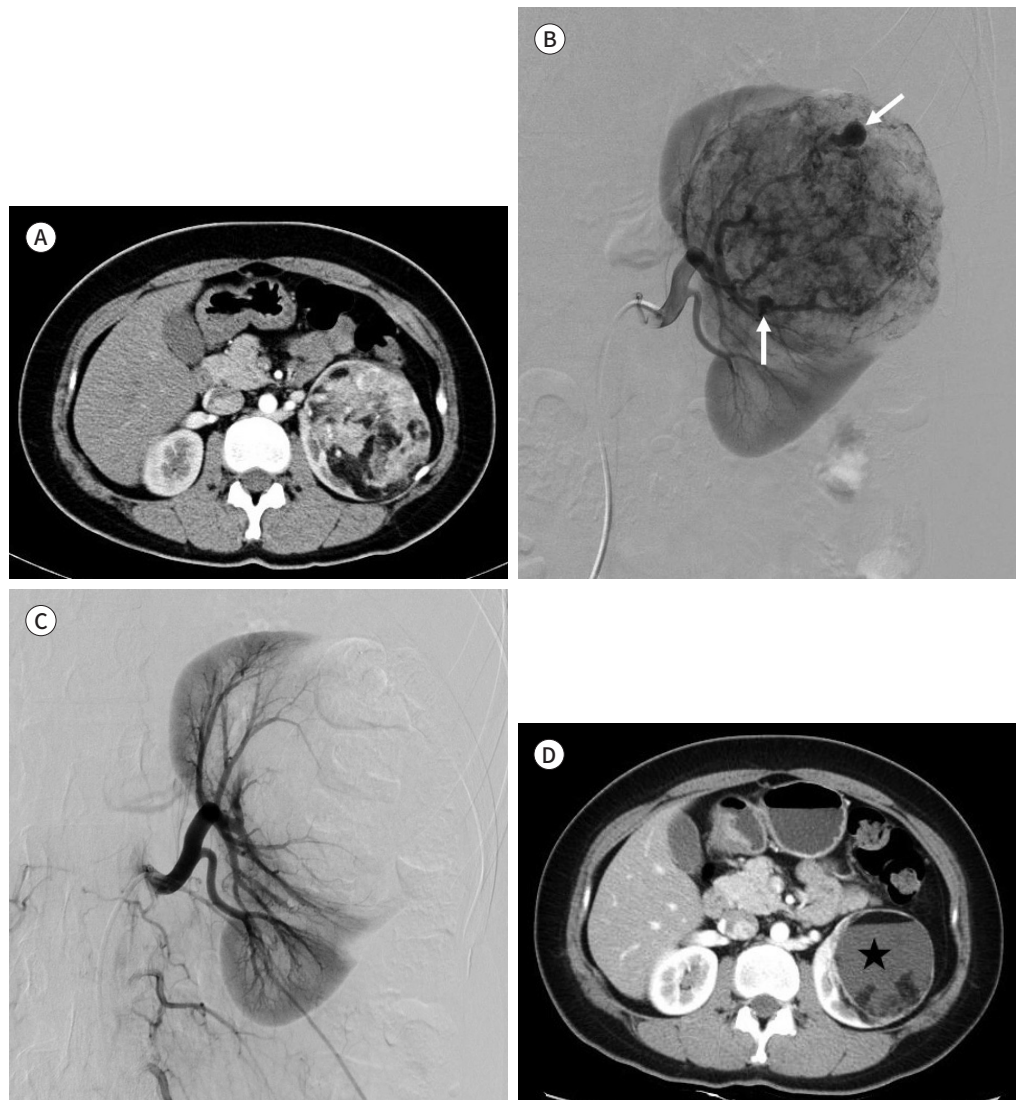
**Fig. 10.** A 31-year-old female with a painful angiomyolipoma.

**A.** CT shows a heterogeneous enhancing mass measuring 8 cm × 7 cm × 8 cm with a fat component in the left kidney.

**B.** Left renal artery angiogram reveals a hypervascular tumor staining with abnormal vasculature and two distinct aneurysms (arrows).

**C.** Angiogram after selective transarterial embolization with polyvinyl alcohol (250–355 μm) and microcoils shows complete devascularization of the tumor.

**D.** Enhanced CT after 1 year shows the fluid-fluid level with fat layering in the residual tumor, indicating liquefaction (star), as well as a decrease in the tumor volume by 35.90%.



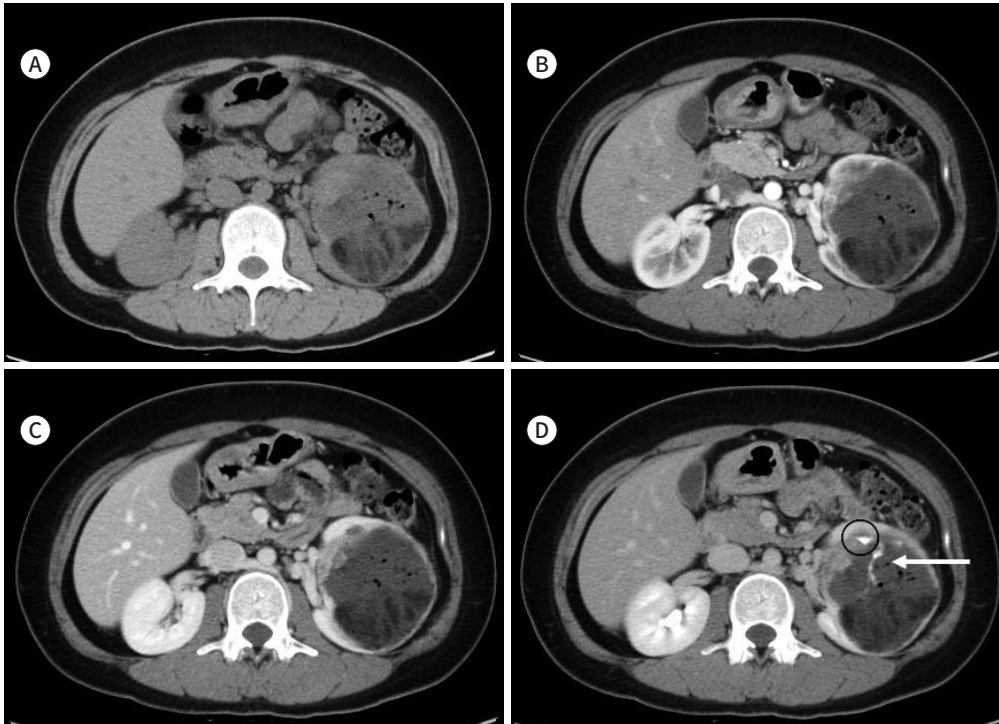
## OUTCOME OF TAE

Long-term outcome of TAE as the first-line treatment for renal AMLs is safe, effective and durable to manage high-risk or symptomatic lesions (7, 11). As in previous studies, TAE achieves complete occlusion of feeding arteries supplying to the AML in 93.9% (28) and 85% of bleeding AMLs were successfully embolized on the first attempt (7).

But, tumor regrowth and rebleeding after embolization remain a concern. Recurrence

**Fig. 11.** A 31-year-old female with transient hematuria occurring immediately after transarterial embolization (same case as that presented in Fig. 10).

**A-D.** CT performed 2 weeks after transarterial embolization shows complete devascularization with multiple punctate air densities, indicating tumor necrosis. Only the excretory phase scan (**D**) reveals contrast extravasation (white arrow) within the lesion, which appears to be connected to a renal calyx (black circle), but no contrast extravasation is observed in the unenhanced (**A**), cortical (**B**), and parenchymal (**C**) phases. The patient had complained of transient fever and left flank pain and had presented leukocytosis, which subsided with conservative treatment, as did the hematuria.



rates of AMLs after TAE varies from about 11% to 40% (4). This is because the clinical settings of the enrolled patients are heterogeneous (sporadic versus associated with TSC, and elective versus emergent situation). Moreover, the recurrence was defined in different ways between studies. Re-embolization or subsequent surgical removal is sometimes required, with 38% retreatment rate after 3 years of TAE (34).

Chan et al. (7) reported that 4 (14.8%) patients required re-embolization and renal surgery was required in 4 (14.8%) for a mean period of 7.1 years. Anis et al. (11) reported that the re-embolization rate was 41.1% and four renal units (5.9%) were eventually treated surgically for 10 years of follow-up. In previous studies, the relatively high rate of repeated procedures seems to be more relevant to the radiological assessment of imaging follow-up rather than recurrent rupture. Recurrent hemorrhagic rupture requiring repeat TAE occurs in only 2.5% (28).

## REPEAT TAE

TAE can be repeated as required. Tumor regrowth or rebleeding do not indicate the need for surgical intervention because the outcomes of repeated TAE are safe, well-tolerable and effective (16).

The repeated procedure is also determined with the radiologic and clinical assessment. On follow-up, the followings should be surveilled: radiologic failures such as incomplete devascularization of AMLs with significant remaining angiomyogenic component and progressive increase in size of tumor with revascularization, and clinical failure such as refractory or recurring symptoms (5, 7, 28).

## TAE VS. SURGICAL REMOVAL

Surgical removal is the most effective treatment of sporadic renal AMLs in terms of recurrence and need for secondary procedures (1). It also has an advantage of being able to exclude malignancy in case of diagnostic uncertainty, and immediately remove the lesion. Nephron-sparing surgery (NSS) offers preservation of renal function and is associated with acceptable complication and low local recurrence rates (3.4%) in sporadic renal angiomyolipoma (35).

However, according to the reported studies, the average dimension of AMLs treated by nephron-sparing surgery was smaller than that treated by TAE (7). Surgical resection of giant AMLs larger than 10 cm would generally require that a greater percentage of the normal renal parenchyma be removed (24).

Although nephron-sparing approach has been performed in the surgical management recently, NSS tends to have more increase in creatinine levels and creates relatively more frequent procedure-related complications compared to TAE (19, 21). Moreover, TAE can be opted in cases with massive, central, or endophytic renal AML that precludes NSS (21). TAE is not only a safe and effective alternative to surgical management, it can also serve as a preoperative adjunct. Also TAE is less costly than surgery. The mean length of hospital stay for TAE is 3 days while it takes 6 days for patients undergoing surgery (5, 13, 35).

## PROCEDURE-RELATED COMPLICATIONS

Postembolization syndrome (PES) is most common complication, affecting as high as 100% (6, 7, 19). PES is attributable to inflammatory mediators released after embolization, which manifests as a flank pain, fever, leukocytosis, and nausea. PES is usually self-limiting and managed by supportive medications.

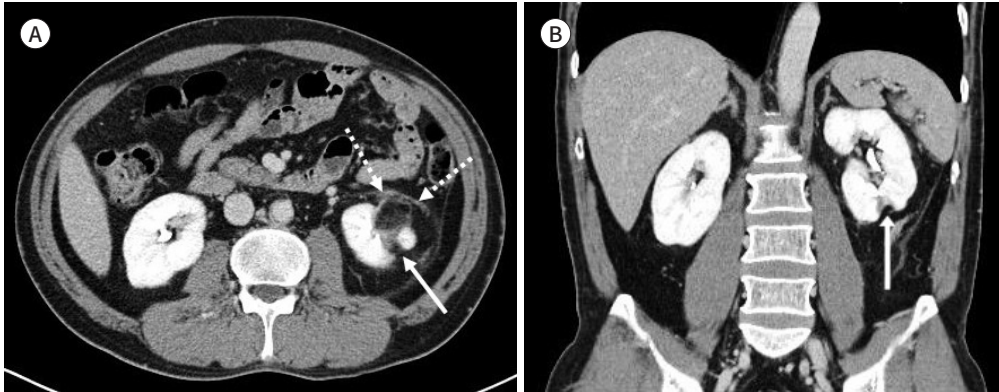
Transient hematuria may occur immediately after TAE, which is thought to be caused by a fistula between the necrotic tumor and the renal calyx, not by arterial bleeding of the residual tumor (Fig. 11).

Previous studies show that TAE preserves renal function with unchanged estimated glomerular filtration rate (eGFR). Temporary insignificant deterioration of renal function immediately after TAE is more likely to be related to the use of contrast agents, and the eGFR does not decline in the long term (19).

It has been reported that renal infarctions after embolization are observed at various frequencies in the follow-up imaging (Fig. 12). But most of them were inconsequential and have no effect on renal function. Sawada et al. (27) reported that focal renal infarction after TAE for renal AMLs was found in 41% (5/12), but the degree of infarction was less than 10%, and no patients exhibit renal insufficiency. Special attention should be also paid to complications

**Fig. 12.** A 50-year-old male with focal renal infarction occurring after embolization (same case as that presented in Fig. 2).

**A, B.** CT performed 3 months after transarterial embolization reveals focal dimpling (arrows) in the normal renal tissue, indicating focal renal infarction and a residual angiomyolipoma mainly composed of fat (dashed arrows). The patient did not show any renal function impairment.



from embolization of extrarenal feeding arteries, such as spinal cord infarction for the intercostal or lumbar arteries and adrenal insufficiency for the adrenal arteries.

Major complications following embolization are rare, but could lead to longer hospital stays. A systemic review reported that major complication occurs in 6.9% of patients, including respiratory complications, pleural effusion, abscess, embolization-induced AML rupture, allergic reactions, urinary retention, urinary tract infection, femoral artery injury requiring repair, and renal artery spasm (5, 28).

With regard to pulmonary complications, potential direct channels into the venous circulation should be kept in mind, even in the absence of visible arteriovenous shunts during angiography (29).

Differentiation between necrotic AML with aseptic liquefaction and abscess is difficult to distinguish because the radiologic appearance is similar (2). Patients should be evaluated clinically with physical examination and laboratory tests to determine if percutaneous drainage is required. Aseptic necrotic liquefaction can be observed without any invasive procedure (Fig. 10).

## CONCLUSION

TAE for renal AMLs is safe, effective and durable in both prophylactic and emergent clinical settings. The target of embolization is the risk factors predictive of tumor bleeding, which should be considered in the patient selection period. The presence and size of aneurysms and the proportion of angiomyogenic component rather than overall tumor size should be assessed on surveillance images. Traditional size threshold (4 cm) for intervention needs to be adjusted upward for better results. In order to achieve optimal therapeutic outcomes, all feeding arteries should be superselected, and a careful infusion of embolic materials (liquid or particulate type) at the distal level should be performed for avoiding nontargeted embolization and an inappropriate early proximal occlusion. These embolization principles apply



equally to an urgent TAE setting for bleeding AMLs in order to prevent tumor regrowth and re-bleeding as well as to arrest ongoing bleeding. The reduction in tumor volume after embolization is closely associated with the initial composition of the AML. From the follow-up images, changes in other radiologic features, such as attenuation within the lesion, proportion of enhancing portion, and abnormal vascularity, together should be assessed as parameters of technical success of TAE. Repeat TAE is also well-tolerable and effective, by reserving further surgical interventions.

### Author Contributions

Conceptualization, C.M.J., K.Y.M.; data curation, C.M.J., J.Y.; formal analysis, all authors; investigation, all authors; project administration, C.M.J.; resources, all authors; supervision, C.M.J.; visualization, C.M.J., J.Y.; writing—original draft, C.M.J., J.Y.; and writing—review & editing, all authors.

### Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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## 산발성 신장 혈관근지방종에 대한 경동맥 색전술: 최적의 치료 결과를 위한 환자 선택 및 기술적 고려 사항

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신장 혈관근지방종은 양성이지만 잠재적으로 생명을 위협할 정도의 후복막강 출혈을 일으킬 수 있으므로 때때로 치료가 필요하다. 경동맥색전술은 혈관근지방종의 출혈성 파열을 예방하고 병변의 비대 또는 출혈로 인한 증상을 완화시킬 수 있는 안전하고 효과적인 치료 방법 중 하나이다. 그러나 산발성 신장 혈관근지방종 환자의 예방적 색전술 시술에 대한 치료 기준에 대해서는 명확한 합의가 없다. 게다가 종양 파열에서 시행하는 응급 시술에서는 임상 증상의 안정화에 초점을 맞춘 불완전한 색전술의 가능성이 있다. 본 임상화보에서는 사례들을 통해 최적의 치료 효과를 위한 환자 선택 및 색전술의 기술적 및 시술 후 고려 사항을 제시하고자 한다.

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